

Aus dem Institut für Hirnforschung der Universität
Zürich (Direktion: Prof. Dr. K. Akert)

THE RANVIER NODES IN THE NEUROGENIC ELECTRIC ORGAN OF
THE KNIFEFISH STERNARCHUS: A FREEZE-ETCHING STUDY ON
THE DISTRIBUTION OF MEMBRANE-ASSOCIATED PARTICLES

INAUGURAL-DISSERTATION

zur Erlangung der Doktorwürde der Medizinischen Fakultät
der Universität Zürich

vorgelegt von

Conrad Ulrich Kristol
von Zürich

Genehmigt auf Antrag von Prof. Dr. K. Akert

Zürich 1980



Research Reports

THE RANVIER NODES IN THE NEUROGENIC ELECTRIC ORGAN OF THE KNIFEFISH *STERNARCHUS*: A FREEZE-ETCHING STUDY ON THE DISTRIBUTION OF MEMBRANE-ASSOCIATED PARTICLES

CONRAD KRISTOL, KONRAD AKERT, CLARA SANDRI, URS R. WYSS, MICHAEL V. L. BENNETT and HANS MOOR

(C.K., K.A., C.S. and U.R.W.) Brain Research Institute, University of Zurich, Zurich CH-8029 (Switzerland), (M.V.L.B.) Division of Cellular Neurobiology, Department of Neuroscience, Rose F. Kennedy Center for Research in Mental Retardation and Human Development, Albert Einstein College of Medicine, Bronx, N.Y. 10461 (U.S.A.) and (H.M.) Laboratory of Electronmicroscopy, Department of General Botany, Swiss Federal Institute of Technology, Zurich (Switzerland)

(Accepted August 20th, 1976)

SUMMARY

The two types of Ranvier nodes (type I with narrow gap, type II with giant gap) and internodes in nerve fibers composing the *Sternarchus* electric organ have been studied by means of freeze-etching electron microscopy. Numerical analysis of the distribution of membrane-associated particles revealed the following features: (1) the P-faces of both types of nodes and of the internodal axon bear a similarly high density of particles (1000–1200 particles/sq. μm on the average). (2) particle density is differential in E-faces: the histogram for type I nodes has a wider range of particle concentrations (114–1522 particles/sq. μm) than that for type II nodes (45–576 particles/sq. μm) whose density values are in the same range as those of the internodal axon. At least some type I nodes (narrow gaps) generate spikes and probably have a low resistivity; these nodes may be those with high particle density on E-faces. The low particle density on E-faces of type II nodes may be associated with high resistivity and absence of excitability. Similarly, the low particle density in internodes may reflect inexcitability. There is evidence that the transition from one nodal type to the next is gradual: as the gap width of type I nodes increases, there is an occurrence of surface elaborations and the density of E-face particles tends to drop towards the range of type II nodes.

INTRODUCTION

Previous investigations using dissection and light microscopic techniques have

established that the electric organ of *Sternarchus* consists of specialized nerve fibers^{4,9,18}. Axons from the ventral roots enter the electric organ, run anteriorly for several segments, turn around and run posteriorly for several segments where they end blindly^{4,30}. Light and electron microscopic studies show that each axon has two main types of Ranvier nodes which differ with respect to localization and structure^{4,29,30}. Nodes with narrow gaps (0.5–1.0 μm) and a relatively smooth axolemma with distinct cytoplasmic undercoating are mainly localized in the proximal and central regions of the anteriorly and posteriorly running segments of the nerve fiber. Nodes with very large gaps (up to 50 μm and more) are situated at the distal regions of anteriorly and posteriorly running segments. These nodes have extensive surface elaborations by irregular polypoid processes and lack cytoplasmic undercoating of the plasmalemma (Fig. 1).

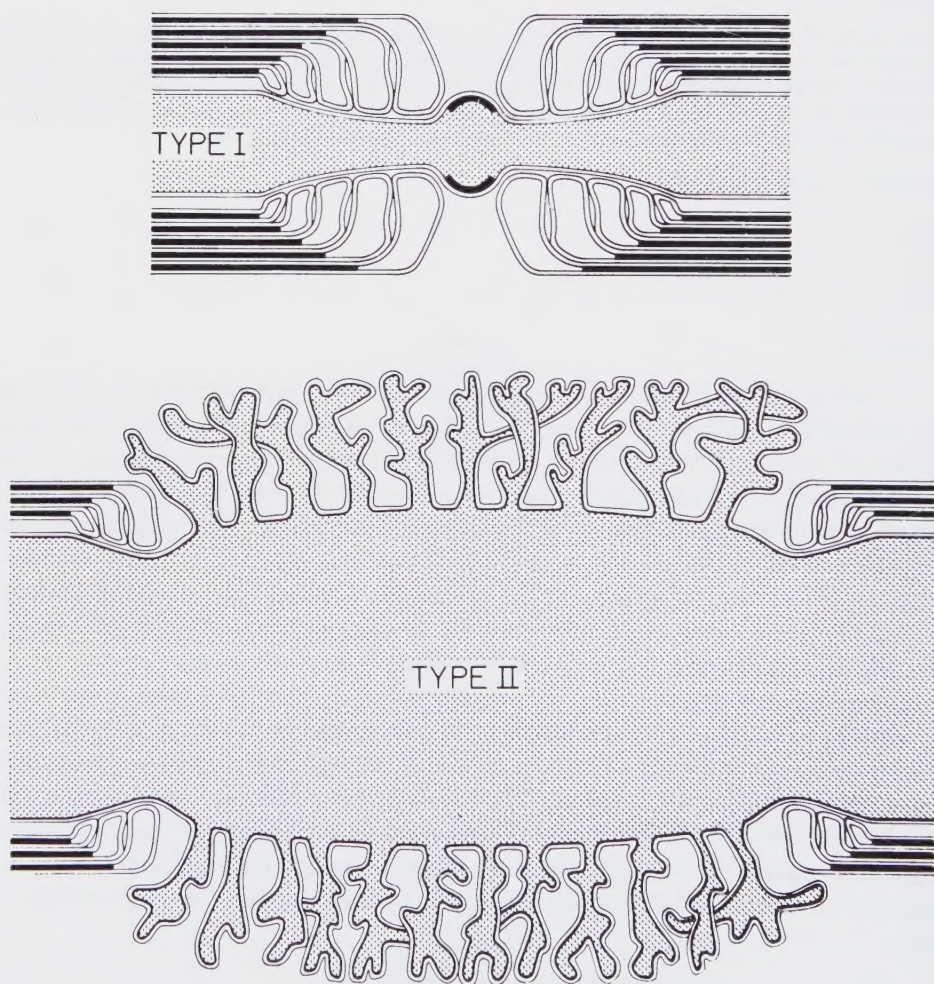


Fig. 1. Diagram summarizing the results of the electron microscopic study by Waxman et al.³⁰. Type I corresponds to a conventional node; type II lacks undercoating of nodal membrane and has a vastly extended surface.

Physiological data indicate that the two nodal types have very different properties^{4,30}. At least some of the nodes with narrow gaps generate the electric discharge and presumably are of low resistivity like the nodes of ordinary myelinated fibers. In contrast the nodes with large gaps have a very high resistivity and act as a series capacity.

These strikingly different properties of the nodes prompted us to study these structures with the freeze-etching technique by which vast membrane faces (although not surfaces) are exposed and amenable to electron microscopic investigations. The main purpose was to examine morphometrically the membrane-associated particles of the nodal zone in both types of node with a view to correlating distributions with physiological properties.

METHODS

The electric organs of 12 *Sternarchus albifrons* were used for this investigation. The animals were anesthetized with MS-222 (Sandoz, Basle). Tissue fixation was achieved with 2.25% glutaraldehyde in Millonig's buffer by intracardiac perfusion or immersion and subsequent washing in the same buffer with 0.5% sucrose. For cryoprotection the tissue blocks were immersed at room temperature in 25% glycerol in Ringer solution for 30 min.

Tiny blocks were then rapidly frozen in liquid freon (-150°C) and kept in liquid nitrogen (-196°C) before being fractured and etched according to the methods of Moor and Mühlethaler¹⁶ and Moor¹⁷ using a Balzers freeze-etching unit Ba 360 M. Replicas were made by evaporation of platinum and carbon. After cleaning with chromic acid of different concentrations the replicas were mounted on formvar coated grids. Electron micrographs were made with Siemens Elmiskop IA and 102. Designation of fracture faces follows the nomenclature proposed by Branton et al.⁸.



Fig. 2. Model applied to the calculations of the surface of nodal membranes. The periaxonal space filled by polypoid elaborations of the nodal surface is represented by a cylindrical shell (below), individual polypoid processes by a cone (above).

A Tektronix graphics Tablet-4953 was used for the morphometric analysis. It was connected to a Tektronix Display Terminal 4010 and a PDP-11 computer. Membrane associated particles were recorded by means of electron micrographs. The original films of freeze-etch replicas (primary magnification $\times 20,000$) were enlarged 6 times. Sample membrane areas were outlined on the grid of a coordinate system that was used for direct computation of particle density per square unit. Membrane areas which were either too small (less than $0.1 \text{ sq. } \mu\text{m}$) or hampered by artifacts, curved edges etc. were excluded. The average sample area was about $0.7 \text{ sq. } \mu\text{m}$. All particles that could be clearly identified were recorded within the sample area (Fig. 15). Reliability was ascertained by repetitive recording of particles within identical areas by the same observer with and without changing the position of the grid of the coordinate system. Results of these tests were examined by the Student *t*-test and failed to show significant differences within identical areas. Results obtained from smaller and larger areas (from 0.2 to $1.0 \text{ sq. } \mu\text{m}$) did not differ significantly. The Student *t*-test was also used for examination of statistical differences between membrane regions.

The polypoid processes entirely fill an approximately cylindrical shell in the nodal zone. The small amount of extracellular space can be seen by inspection of Fig. 9. From the surface to volume ratio for two possible geometries of the processes and from the volume of the shell we obtain the total surface of the processes which is then compared to the surface for a smooth node without processes. If the polypoid processes are cylindrical with a length, l , that is long compared to their radius, ρ , we can neglect the area of the ends and obtain for the ratio of area to volume, Q :

$$Q = \frac{2 \cdot \pi \cdot \rho \cdot l}{\pi \cdot \rho^2 \cdot l} = \frac{2}{\rho}$$

If the processes are conical with side length, l , large compared to the radius of the base, ρ (Fig. 2) then:

$$Q = \frac{3 \cdot \pi \cdot \rho \cdot l}{\pi \cdot \rho^2 \cdot \sqrt{l^2 - \rho^2}} \cong \frac{3}{\rho}$$

For outer and inner radii, R and r respectively, and nodal length, d , the volume, V , occupied by polypoid processes is:

$$V = \pi \cdot (R^2 - r^2) \cdot d$$

the surface, S , of a smooth node of radius, r , is:

$$S = 2 \cdot \pi \cdot r \cdot d$$

and the increase, τ , in surface produced by polypoid processes would be for cylindrical geometry:

$$\tau = Q \cdot \frac{V}{S} = \frac{R^2 - r^2}{r \cdot \rho}$$

and for conical geometry:

$$\tau = \frac{3}{2} \cdot \frac{R^2 - r^2}{r \cdot \rho}$$

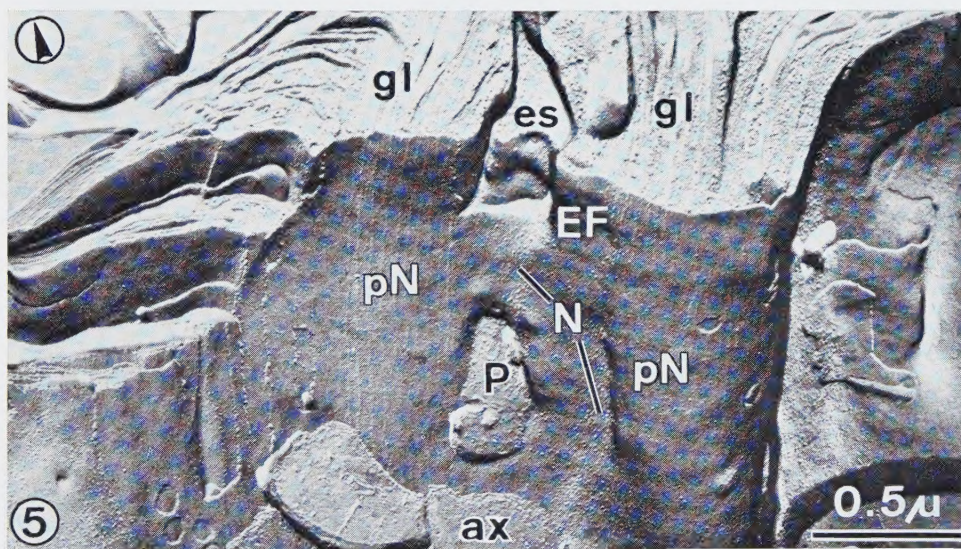
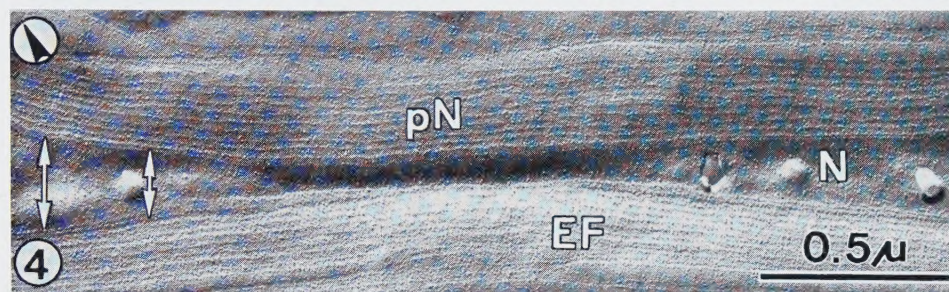
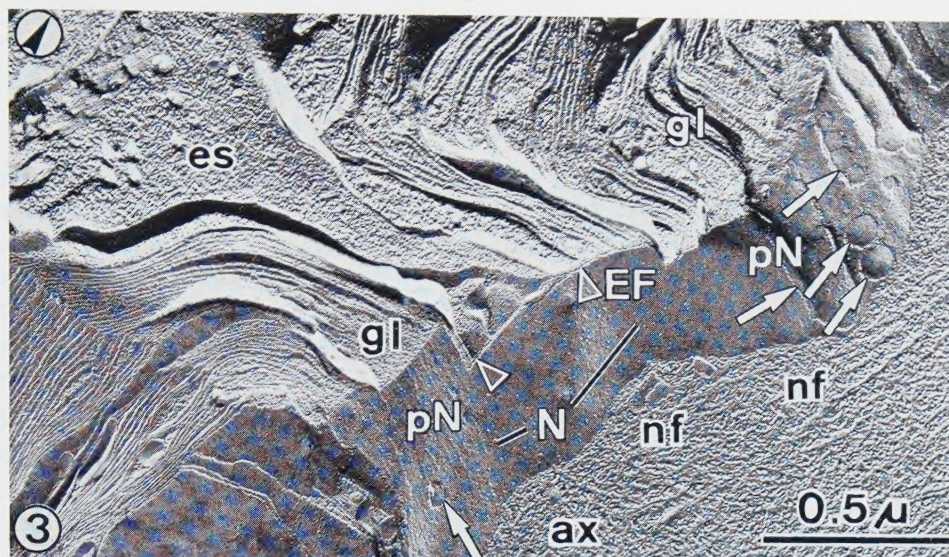


Fig. 3. Axonal E-face (EF) of a smaller gap type I node without surface elaborations. The extent of the nodal zone (N) is marked by arrowheads. The particles form irregular patches and are not readily seen for technical reasons (low degree of etching). The paranodal zone (pN) is characterized by narrowly spread parallel lines of particles lying opposite the overlying Schwann cell loops. The Schwann cell loops (gl) are exposed by irregular defects of the axonal membrane (arrows). These are probably regions of close contact between Schwann cell and axon. The axoplasm (ax) contains neurofilaments (nf). The encircled arrow in this and the following micrographs indicates the direction of shadowing. es = extracellular space. Magnification: $\times 50,000$.

Fig. 4. Axonal E-face (EF) of a smaller gap type I node. The paranodal zone (pN) is clearly marked by the parallel lines of particles. Arrows indicate the variation of gap width. The nodal zone (N) is characterized by a relatively high density of intramembranous particles. Magnification: $\times 50,000$.

Fig. 5. Axonal E-face (EF) of a larger gap type I node (N) with a moderate density of particles. Nodal processes (P) of the axon are present. Both paranodal zones (pN) are identified by typical parallel lines of particles indicating the specialized junction between Schwann cell (gl) and axon. es = extracellular space; ax = axoplasm. Magnification: $\times 40,000$.

The latter estimate is 1.5 times the former. The calculation is independent of the length and number of processes and moderate curvature would not be of great importance. Also a moderate degree of branching would have no major effect.

RESULTS

Nodes with narrow gaps (type I)

The nodal membrane is generally flat and smooth. Nevertheless, there are occasional bulbous protrusions from the axon to the extracellular space (Figs. 5, 6).

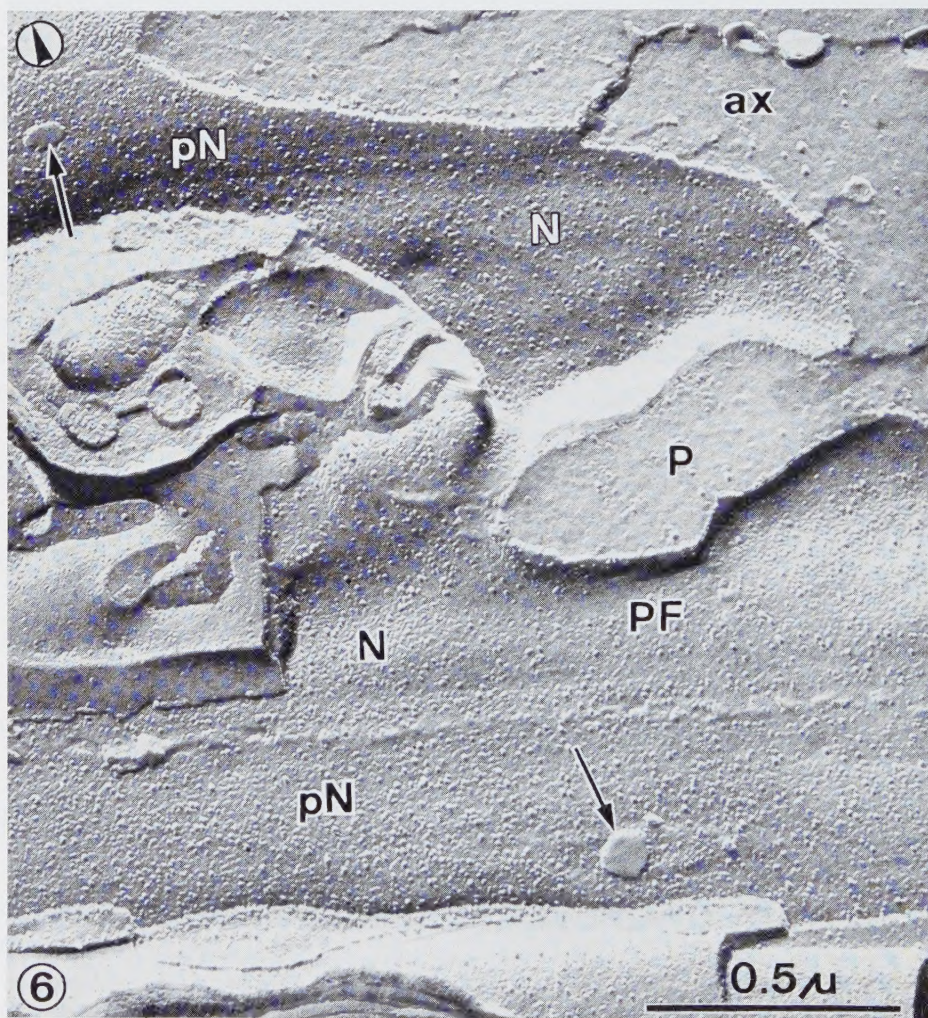


Fig. 6. Axonal P-face (PF) of larger gap type I node with a large nodal process (P) on the right side. The distribution of particles is regular and of high density. On the paranodal P-face (pN) particles are less clearly arranged in parallel lines than on the E-face. Patches of glial membrane (arrows) indicate the attachment of glial and axonal membranes in the paranodal region. ax = axoplasm. Magnification: $\times 66,000$.

The oval or round profiles of the processes have diameters from about 0.2 to 0.7 μm measured at the level of the axon cylinder. The length of these processes could not be ascertained: however, they seem relatively short (about half the thickness of the myelin sheath) and fail to ramify. These axonal elaborations are not to be confounded with finger-like processes derived from the Schwann cells²⁵ which are normally seen in the nodal area. A relationship between the width of the nodal area and the occurrence of processes seems to exist, the smaller nodes (gap width about 0.5 μm) being smooth or equipped with only few processes, the larger nodes (gap width about 1.0–1.5 μm) generally having a moderate number of processes.

Membrane-associated particles (7–15 nm) are randomly distributed and of high density at the P-face, i.e. the inner face of the cytoplasmic membrane leaflet (Figs. 6, 10). On the E-face, i.e. the inner face of the outer leaflet (Figs. 3–5), the particles are less densely and more irregularly distributed than at the P-face. The distribution of E-face particles differs among nodes; there are particle-rich and particle-poor nodes (Table I). This aspect will be taken up further below.

Nodes with giant gaps and surface elaborations (type II)

The nodal zone extends 50 μm and more along the axon; it is characterized by impressive surface elaborations (Fig. 9) of virtually thousands of processes^{29,30}. There are also shorter nodes of about 10 μm with the same nodal structure. Proximal diameters of polypoid processes (Figs. 7, 8) vary from less than 0.2 μm up to more than 1 μm , distal diameters from about 0.05 μm to 0.5 μm . The processes are seen to form secondary and tertiary branches (Fig. 9).

Membrane-associated particles are of about the same size as in type I nodes (7–15 nm). The distribution of particles shows differences between the two fracture faces, the P-face being particle-rich, the E-face being particle-poor (Figs. 12, 13). No regional differences within nodal membrane areas and no differences between giant nodes could be established.

Density of membrane-associated particles in the nodal and internodal segments

P-face. The average density of particles is generally higher on the P-face than on the E-face (Table I). The histograms of P-faces (Fig. 16A, 16D) reveal an even dispersion between 800 and 2000 particles/sq. μm in both types of nodes.

E-face. Distributions of particles on the E-face are strikingly different in the two types of node ($P < 0.005$) (Table I). The density distribution of type I (Fig. 16B) reveals a large dispersion between 114 and 1522 particles/sq. μm . The distribution shows two prominent elevations, one at about 400 particles/sq. μm and a second at 800–1000 particles/sq. μm .

In type II (Fig. 16E) the density ranges between 45 and 576 particles/sq. μm with a peak value of about 300 particles/sq. μm which is close to the first peak of type I.

Counts ($N = 19$) from the *internodal axonal membrane* (Table I, Figs. 16C and F) reveal a low density of particles on the E-face (around 300 particles/sq. μm) and a high density on the P-face (around 800 particles/sq. μm). Thus, the P-face of the axonal membrane, both nodal and internodal, seems to be relatively uniform with

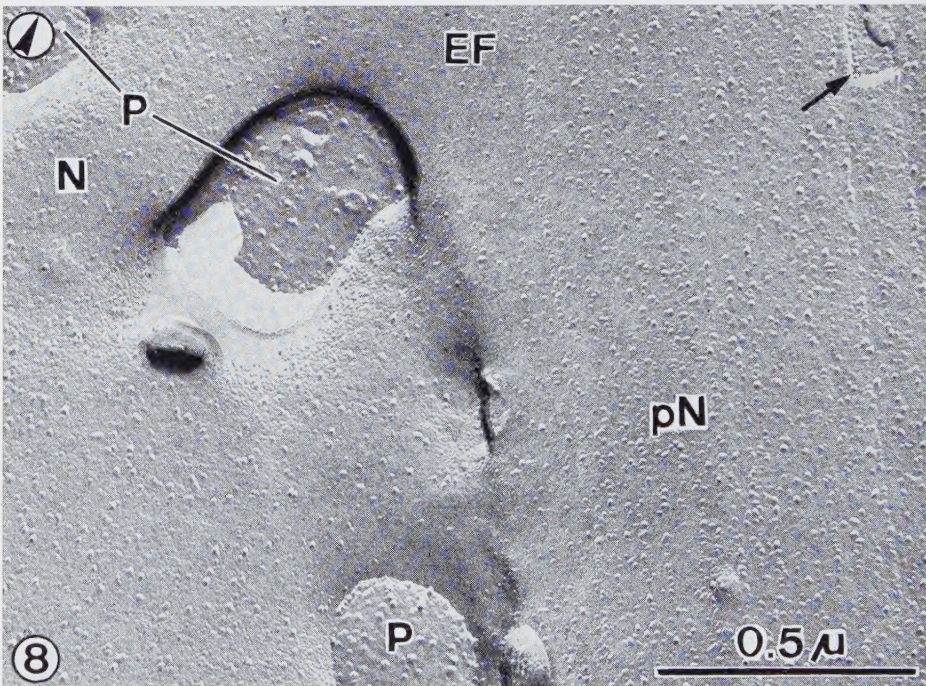
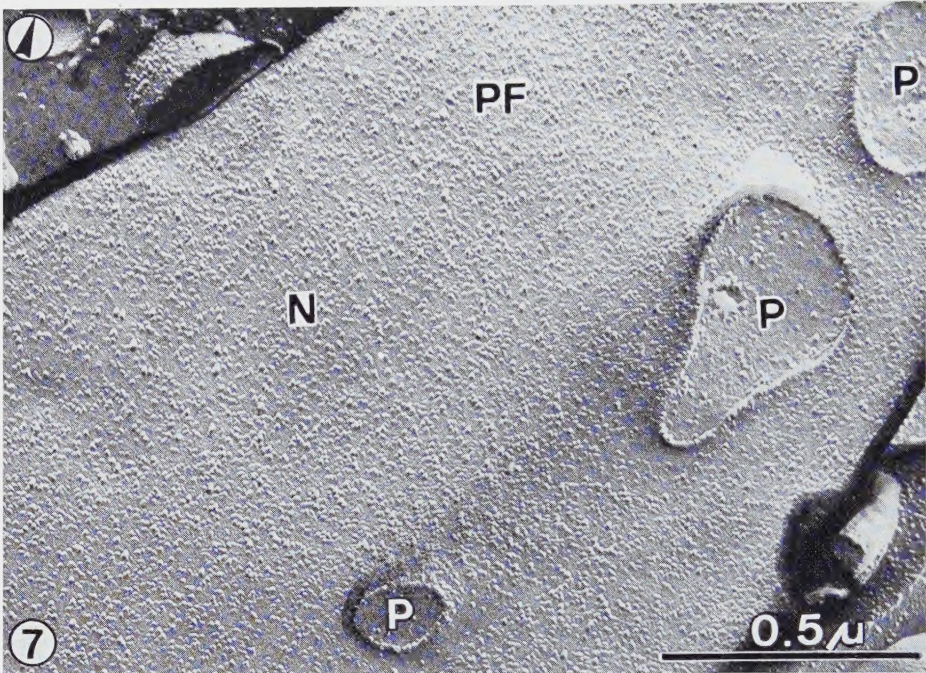


Fig. 7. Axonal P-face (PF) of a type II node showing exit of processes at the level of the axon cylinder. Three stem processes (P) are visible. The node (N) has a high density of particles. Magnification: $\times 68,000$.

Fig. 8. Axonal E-face of type II node (EF) with a few processes (P) at the level of the axon cylinder. The nodal zone (N) is particle-poor, the paranodal zone (pN) reveals the same linear arrangement of particles as observed in Figs. 2-4. The particle rows stand out more clearly if viewed when the micrograph is tilted. Irregular fracture lines (arrow) of the paranodal membrane indicate adhesion between glial and axonal membranes. Magnification: $\times 68,000$.

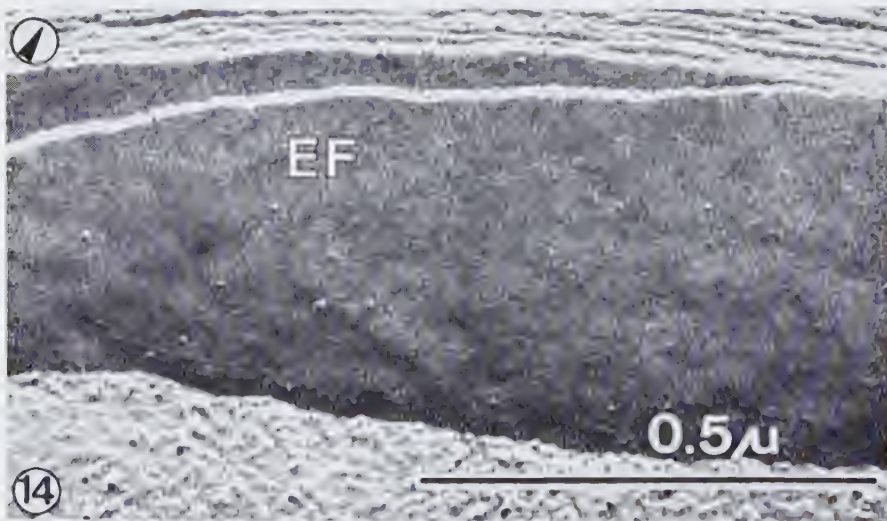
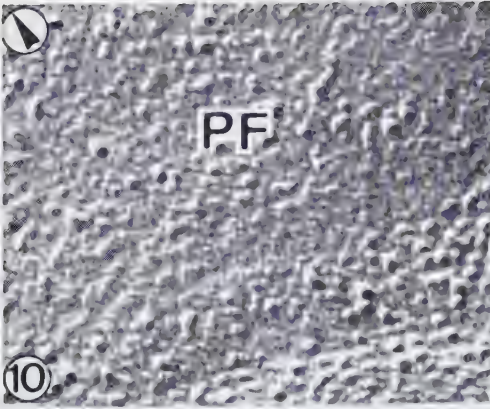
respect to membrane-associated particles. E-face values of internodal axon correspond to those of the particle-poor type II nodes.

Nodal surface in type I vs. type II nodes

The values of axonal diameter and width of the nodal gap for surface determination (Table II) are taken from Waxman et al.³⁰: type I with a gap of about $1.0\ \mu\text{m}$ has an axon diameter of $20\text{--}100\ \mu\text{m}$, depending on its location in small or enlarged parts of the fiber. Type II with a giant nodal gap of $50\ \mu\text{m}$ has an axon diameter of $100\ \mu\text{m}$ and polypoid branches extending radially about $4\ \mu\text{m}$. The average diameter of a single process is about $0.35\ \mu\text{m}$ (our own measurement).



Fig. 9. Type II node fractured nearly longitudinally with polypoid axonal processes exposing concave E-faces (EF) and convex P-faces (PF). Arrows indicate points of bifurcation. At the bottom of the picture the cytoplasm of the main axon (ax) is visible. The particle density is lower in E- than in P-faces (see also Figs. 12–13). Magnification: $\times 52,000$.



Figs. 10–14. Nodal membranes of type I (Figs. 10 and 11) and of type II (Figs. 12 and 13). The axonal P-faces (PF) are consistently particle-rich (1000–1200 particles/sq. μm). The E-faces (EF) are more differentiated. The type I has a particle-rich E-face (Fig. 11); the type II has a particle-poor E-face (Fig. 13). The E-face of the internodal zone (Fig. 14) is also particle-poor. Magnification of all samples is $\times 120,000$.

NUMBER OF POINTS 358
 SURFACE 0.2351
 DENSITY OF POINTS 1522.7625

NUMBER OF POINTS 205
 SURFACE 0.5606
 DENSITY OF POINTS 365.6852

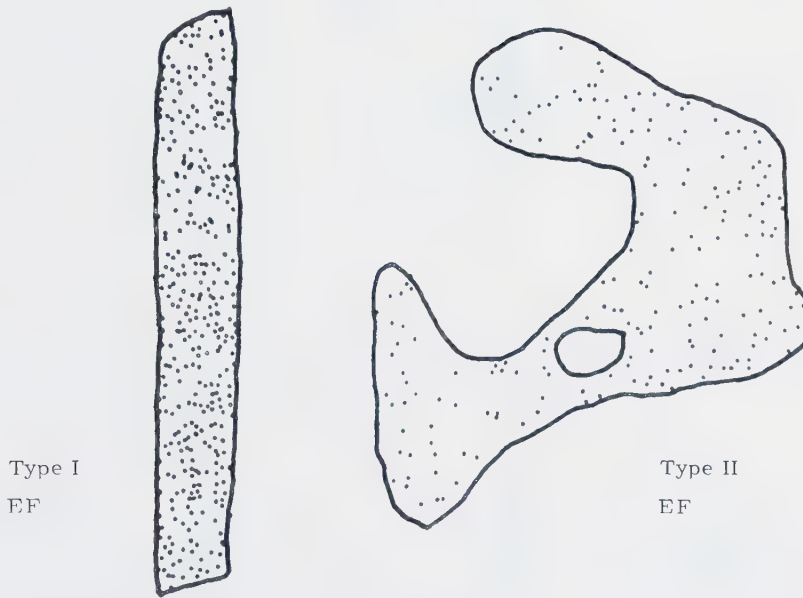


Fig. 15. Samples of the computer readout indicating the number of recorded particles (dots), the surface area in sq. μm and the particle density in number per sq. μm . The E-face of the type I node is an example of a particle-rich membrane face. The E-face of the type II has a low particle density. Magnification of both samples is $\times 58,000$.

TABLE I

Average particle densities of the different membrane areas with standard deviations and coefficients of variation

Note the exceptionally high coefficient of variation for the E-face of type I nodes and the low variation for the E-faces of internodes and type II nodes.

Membrane face		Average (part./sq. μm)	Standard deviation (Part./sq. μm)		N
				Coeff. of variation	
Type I node	P-face	1054.6	238.6	0.226	14
	E-face (total)	599.8	336.7	0.561	33
	E-face (first peak)	394.8	108.2	0.274	22
	E-face (second peak)	1009.7	246.9	0.245	11
Type II node	P-face	1230.4	363.4	0.295	20
	E-face	308.2	116.3	0.377	19
Internode	P-face	828.0	104.9	0.127	4
	E-face	295.3	109.6	0.371	15

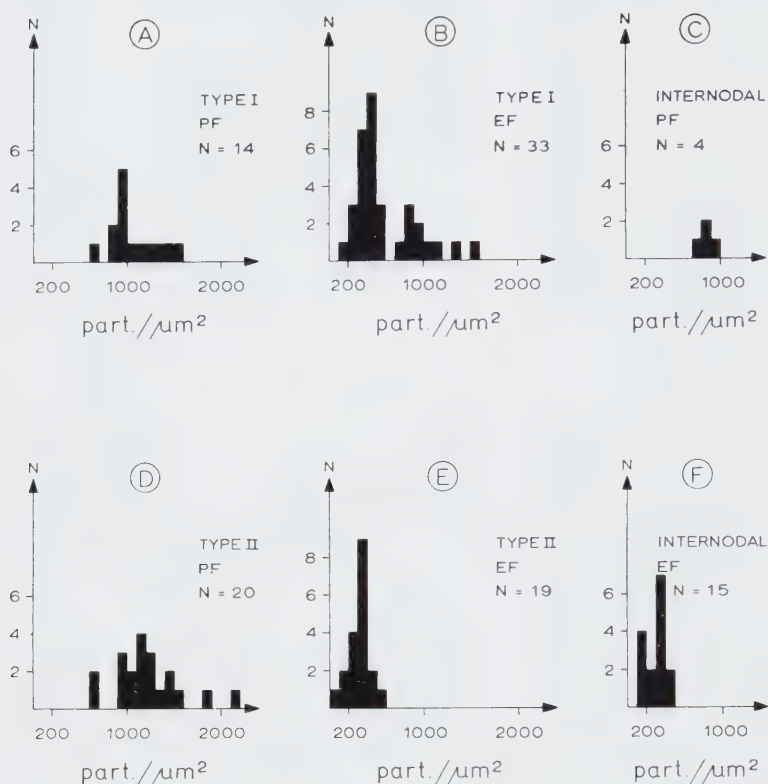


Fig. 16. Histograms of distribution of particle density. The P-faces are not greatly different, whereas the E-faces reveal characteristic differences. Note that E-faces of type II nodes and internodes have similarly low particle concentrations, while the E-face of one group of type I nodes is strikingly particle-rich. N = number of areas sampled as shown in Fig. 15. PF = P-face; EF = E-face.

Calculations were made on the basis of the method described in Fig. 2. The surface increase of type II versus type I in regions of small fiber diameter is primarily due to the larger nodal dimensions (a factor of $250 \times$). A further increase by a factor of $50\text{--}70 \times$ is brought about by the polypoid processes (cylindrical and conical processes respectively). Thus, the total surface increase is by a factor of about 12,000–18,000.

TABLE II

Surfaces of type I vs. type II nodes calculated by the method explained in Fig. 2

For further explanation see text.

Type of node	Nodal surface (sq. μm)
Type I (small diameter)	60
Type I (large diameter)	300
Type II (giant gap)	800,000–1,200,000

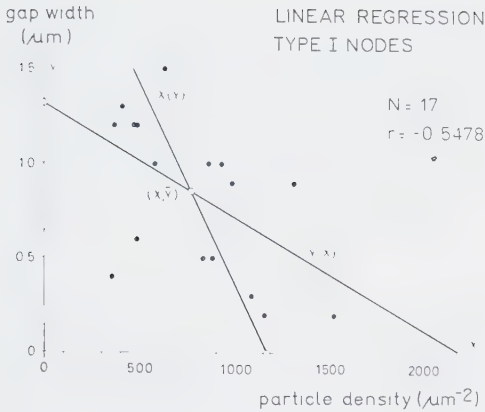


Fig. 17. Linear regression model for two random variables, particle density (X) and gap width (Y), of type I nodes. Although the correlation coefficient $r = -0.5478$ is low, the zero-correlation hypothesis may be rejected (confidence limit 0.95), and the two-dimensional distribution of the variables indicates a negative correlation between particle density and gap size.

Correlation between nodal type and particle distribution

The correlation between nodal size and particle distribution was examined in detail for type I nodes because the histogram (Fig. 16B) of E-face particle distribution was not uniform and extended over a wide range. Seventeen nodes of type I were analyzed and the results are shown in Fig. 17. Narrower gaps have a tendency to correlate with high particle densities, while nodes with increasing gap size seem to have lower density values. This tendency is clearly reflected in the negative direction of the regression line. The correlation coefficient, however, has a low value.

The correlation between gap size and particle density on the E-face of type II nodes was not obtained for technical reasons. However, this type of node is well characterized by its giant size and the presence of processes, and the histogram (Fig. 16E) demonstrates a relatively uniform distribution of particles in the very low range. Thus the correlation between nodal type and particle distribution seems sufficiently established.

DISCUSSION

The present investigations confirm and extend types of nodal morphology previously described³⁰. The geometry of type II surface elaborations with their branching is more clearly visible in electron micrographs of freeze-etching replicas than in individual thin sections. New features have been added by analyzing the membrane-associated particles and their distribution in the nodal regions. Distributions of density of nodal particles are significantly different in type I and II nodes. These differences are limited to the E-faces (outer membrane leaflet) and fail to exist in P-faces (inner membrane leaflet). The much wider density distribution of E-face particles in type I and the occurrence of two apparent nodes suggest that more than one type of node is included in what is now designated as type I. At least one group

of type I nodes seems characterized by a low density of particles which is similar to that seen in type II. This similarity with type II exists also to some extent with respect to the increased width of the gap. Conceivably, this group of nodes belongs to regions where the fibers are of larger size and their myelin sheath is thinner as described for type II nodes by Waxman et al.³⁰ On the other hand, the surface of this group of type I nodes with somewhat larger gap is far less elaborated than that of type II nodes. Therefore, we consider it (further comments below) as transitional between type I with small gap and type II with giant gap.

The thickness of the myelin sheath may be a useful indication of transition between different nodal types. Maxwell et al.¹⁴ have described a sudden reduction in the thickness of myelin in the transition zone (so-called Obersteiner-Redlich zone) from the peripheral to central myelin of the trigeminal nerve root. This reduction takes place at a single node of Ranvier and corresponds to the change from Schwann to glial cell investment. In the electric organ of *Sternarchus*, all the myelin is formed by Schwann cells, and the thickness of the myelin sheath appears to change gradually from node to node.

Because of physiological and morphological differences between type I and II nodes it is tempting to ascribe functions for the membrane-associated particles observed. The P-face particles, which do not differ significantly in either type of node or in internodal regions, may mediate functions common to all membranes such as ubiquitous plasmalemmal enzymes and antigenic sites. The differences in E-face particles may represent in part different distributions of ionic channels for Na and K. At least some of the type I nodes must be excitable^{4,30}. Presumably they are of low resistivity like other nodes and have a high density of Na and K channels which may appear as E-face particles. The type II nodes are of high resistivity and inexcitable; the density of E-face particles is low. To be sure the total number of E-face particles is larger than at type I nodes and it is unlikely that all E-face particles are channels. There is evidence from mammalian fibers that internodal membranes are inexcitable²⁴. In *Sternarchus* axons they have few E-face particles.

Type I nodes in the large diameter regions of the fiber may have membrane properties similar to those of type II nodes. The small size of these nodes compared to type II nodes would function in extending the length of the dipole equivalent of the active fiber segment. Inexcitable type I nodes could account for the transitional forms with few E-face particles.

The high density of E-face particles in type I nodes is well above the range proposed for Na channels of nodal membranes^{2,13,28}. This fact suggests that E-face particles are not exclusively channels for action currents, but may also represent other molecules as for example the Na pump. The particles do vary in size which may reflect structural and functional diversity.

Association of E-face particles with ionic channels is suggested by the highly specialized particle aggregations on the E-face of postsynaptic membrane at chemical synapses²⁶ and the motor endplate^{10,12,20}. Particle aggregates are characteristic of gap junctions, which contain hydrophilic channels connecting the cells^{6,11,15}. The aggregates occur in E-faces in arthropods, but they are found in the P-faces of these junc-

tions in all other groups examined to date¹¹. Membranes in the *Fundulus* embryo show correlations between particles and resistivity⁷. The plasma membrane facing the external environment is of very high resistivity and is quite impermeable; this membrane is virtually devoid of particles. The membrane surrounding the yolk vacuole is of high resistivity but has many particles on both E- and P-faces; presumably it is active in transporting nutritive substances. Other surface membranes of normal resistivity have numerous particles in both E- and P-faces. These data suggest that membrane-associated particles may be necessary for low resistivity, but that high resistivity membranes can have particles. Additional cells that could be investigated to correlate resistivity with particle distribution are receptor cells of phasic electroreceptors⁵ and certain myogenic electrocytes in which one face is of low resistivity and electrically excitable and one face is of high resistivity and inexcitable^{3,4,27}.

A further characteristic difference between nodal types in *Sternarchus* is in respect to cytoplasmic undercoating which is present in type I nodes and absent in type II nodes³⁰. Such cytoplasmic undercoating of the axoplasm has been described at ordinary nodes of Ranvier^{1,21} as well as at the initial segment^{19,22}.

Recently it was found in both myelinated fibers of rat sciatic and *Sternarchus* electrocytes that regions with cytoplasmic undercoating stain preferentially with a technique of successive ferric and ferrocyanide treatments²³. However, the technique did not illuminate questions of gradations between type I and type II nodes and of different excitability in different type I nodes.

All of these findings taken together suggest that cytoplasmic undercoating of the axolemma and increased density of E-face particles may be morphological specializations that are in some way related to the production of electrical signals.

ACKNOWLEDGEMENTS

This work is supported by grants of the Swiss National Foundation for Scientific Research Nr. 3.368.0.74, 3.774.72 and 3.045.72, the Hartmann-Müller Foundation for Medical Research, the Dr. Eric Slack-Gyr Foundation and the EMDO-Stiftung in Zurich and by NIH Grants (supporting M. V. L. Bennett) HD-04248 and NB-07512.

The skillful assistance of Mr. A. Fähr, Mr. D. Savini, Miss R. Emch and Miss U. Fischer is gratefully acknowledged.

REFERENCES

- 1 Andres, K. H., Ueber die Feinstruktur besonderer Einrichtungen in markhaltigen Nervenfasern des Kleinhirns der Ratte, *Z. Zellforsch.*, 65 (1965) 701-712.
- 2 Armstrong, C. M., Ionic pores, gates and gating currents, *Quart. Rev. Biophys.*, 7 (1975) 179-210.
- 3 Bennett, M. V. L., Comparative physiology: electric organs, *Ann. Rev. Physiol.*, 32 (1970) 471-528.
- 4 Bennett, M. V. L., Electric organs. In W. S. Hoar and D. J. Randall (Eds.), *Fish Physiology*, Vol. 5, Academic Press, New York, 1971, pp. 347-491.
- 5 Bennett, M. V. L., Electrorception. In W. S. Hoar and D. J. Randall (Eds.), *Fish Physiology*, Vol. 5, Academic Press, New York, 1971, pp. 493-574.
- 6 Bennett, M. V. L., Function of electrotonic junctions in embryonic and adult tissues, *Fed. Proc.*, 32 (1973) 65-75.

- 7 Bennett, M. V. L. and Gilula, N. B., Membranes and junctions in developing *Fundulus* embryos, freeze fracture and electrophysiology, *J. Cell Biol.*, 63 (1974) 21a (abstr.).
- 8 Branton, D., Bullivant, S., Gilula, N. B., Karnovsky, M. J., Moor, H., Mühlethaler, K., Northcote, D. H., Packer, L., Satir, B., Satir, P., Speth, V., Staehelin, L. A., Steere, R. L. and Weinstein, R. S., Freeze-etching nomenclature, *Science*, 190 (1975) 54–56.
- 9 Couceiro, A., Leao, A. A. P. and Oliveira Castro, G. de, Some data on the structure of the electric organ of the Itui (*Sternarchus albrifrons* L.), *An. Acad. bras. Cienc.*, 27 (1955) 323–328.
- 10 Dreyer, F., Peper, K., Akert, K., Sandri, C. and Moor, H., Ultrastructure of the 'active zone' in the frog neuromuscular junction, *Brain Research*, 62 (1973) 373–380.
- 11 Gilula, N. B., Junctions between cells. In R. P. Cox (Ed.), *Cell Communication*, Wiley, New York, 1974, pp. 1–29.
- 12 Heuser, J. E., Reese, T. S. and Landis, D. M. D., Functional changes in frog neuromuscular junctions studied with freeze-fracture, *J. Neurocytol.*, 3 (1974) 109–131.
- 13 Hille, B., Ionic channels in nerve membranes. In J. A. V. Butler and D. Noble (Eds.), *Progress in Biophysics and Molecular Biology*, Vol. 21, Pergamon Press, Oxford, 1970, pp. 3–32.
- 14 Maxwell, D. S., Kruger, L. and Pineda, A., The trigeminal nerve root with special reference to the central-peripheral transition zone: an electron microscope study in the Macaque, *Anat. Rec.*, 164 (1969) 113–126.
- 15 McNutt, N. S. and Weinstein, R. S., The ultrastructure of the nexus. A correlated thin-section and freeze-cleave study, *J. Cell Biol.*, 47 (1970) 666–688.
- 16 Moor, H. and Mühlethaler, K., Fine structure in frozen-etched yeast cells, *J. Cell Biol.*, 17 (1963) 609–628.
- 17 Moor, H., Recent progress in the freeze-etching technique, *Phil. Trans. B*, 261 (1971) 121–131.
- 18 Oliveira Castro, G. de, Differentiated nervous fibers that constitute the electric organ of *Sternarchus albrifrons* L., *An. Acad. bras. Cienc.*, 27 (1955) 557–562.
- 19 Palay, S. L., Sotelo, C., Peters, S. and Orkand, P. M., The axon hillock and the initial segment, *J. Cell Biol.*, 38 (1968) 193–201.
- 20 Peper, K., Dreyer, F., Sandri, C., Akert, K. and Moor, H., Structure and ultrastructure of the frog motor endplate, a freeze-etching study, *Cell Tiss. Res.*, 149 (1974) 437–455.
- 21 Peters, A., The node of Ranvier in the central nervous system, *Quart. J. exp. Physiol.*, 51 (1966) 229–236.
- 22 Peters, A., Proskauer, C. C. and Kaiserman-Abramof, I. R., The small pyramidal neuron of the rat cerebral cortex: the axon hillock and initial segment, *J. Cell Biol.*, 39 (1968) 604–619.
- 23 Quick, D. C. and Waxman, S. G., Specific staining of the axon membrane at nodes of Ranvier with ferric ion and ferrocyanide, in press.
- 24 Rasminsky, M. and Sears, T. A., Internodal conduction in undissected demyelinated nerve fibers, *J. Physiol.*, (Lond.) 227 (1972) 323–350.
- 25 Robertson, J. D., Preliminary observations on the ultrastructure of nodes of Ranvier, *Z. Zellforsch.*, 50 (1959) 553–560.
- 26 Sandri, C., Akert, K., Livingston, R. B. and Moor, H., Particle aggregations at specialized sites in freeze-etched postsynaptic membranes, *Brain Research*, 41 (1972) 1–16.
- 27 Schwartz, I. R., Pappas, G. D. and Bennett, M. V. L., The fine structure of electrocytes in weakly electric teleosts, *J. Neurocytol.*, 4 (1975) 87–114.
- 28 Ulbricht, W., Ionic channels through the axon membrane (a review), *Biophys. Struct. Mechanism*, 1 (1974) 1–16.
- 29 Waxman, S. G., Regional differentiation of the axon: a review with special reference to the concept of the multiplex neuron, *Brain Research*, 47 (1972) 269–288.
- 30 Waxman, S. G., Pappas, G. D. and Bennett, M. V. L., Morphological correlates of functional differentiation of nodes of Ranvier along single fibers in the neurogenic electric organ of the knife fish *Sternarchus*, *J. Cell Biol.*, 53 (1972) 210–224.

Curriculum vitae

Ich wurde am 29. März 1953 als Bürger der Stadt Zürich in Zürich geboren. Während 6 Jahren besuchte ich in Zürich die Primarschule und anschliessend während 6 $\frac{1}{2}$ Jahren das Realgymnasium Zürichberg-Rämibühl, das ich im Herbst 1972 mit der Matur Typ B abschloss.

Im Herbst 1972 begann ich das Medizinstudium an der Universität Zürich. Im Sommer 1973 bestand ich das erste, im Frühling 1975 das zweite propädeutische Examen. Anschliessend arbeitete ich während eines halben Jahres am Institut für Hirnforschung der Universität Zürich (Direktion: Prof. Dr. K. Akert). Im Herbst 1975 setzte ich mein Studium fort und bestand im Sommer 1976 das dritte propädeutische Examen und im Herbst 1979 das Staatsexamen.

